

REMARKS

I. INTRODUCTION

The drawings of the present application have been amended as provided above and on the attached Replacement Sheets to clarify the subject matter recited therein and address the Examiner's comments in the Office Action. It is respectfully asserted that no new matter has been added. Support for the amendment to the Drawings can be found in the originally-filed application, including the specification, drawings and/or claims thereof. (See, *e.g.*, originally-filed Figures 1, 3 and 4).

The Specification of the present application has been amended as provided herein above to address certain alleged informalities, and the Examiner's comments provided in the Office Action. It is respectfully asserted that no new matter has been added. Support for the amendment to the specification can be found in the originally-filed application, including the specification, drawings and/or claims thereof. (See, *e.g.*, Specification of the above-identified application, p. 10, Ins. 17-21 p. 19, Ins. 18-29 and p. 30, Ins. 2-12, and originally-filed Figures 1, 3 and 4).

Claims 1, 41-55 and 83 have been amended as provided above to clarify the subject matter recited therein, and to address the Examiner's comments, but not for any reason related to the patentability thereof. Claims 2-40 and 84-122 have previously been cancelled, without prejudice. Applicants hereby reserve the rights to pursue the subject matter recited in the cancelled claims in the present application and/or one or more continuing applications claiming priority from the present application. New claims 123-138 have been added.

Accordingly, claims 1, 41-55, 83 and 123-138 are now under consideration in the above-identified application. Provided above, please find a claim listing indicating the current amendments to claims 1, 41-55 and 83, the addition of new claims 123-138, and the status of other claims on separate sheets so as to comply with the requirements set forth in 37 C.F.R. § 1.121. It is respectfully asserted that no new matter has been added. Exemplary support for the amendments to claims 11, 41-55 and 83, and for the addition of new claims 123-138 can be found in the originally-filed application, including the specification, drawings and/or claims thereof. (See, e.g., Specification of the above-identified application, p. 12, ln. 13 – p. 13, ln. 8, and originally-filed claims 1, 14, 15, 20, 41-55 and 83).

II. **OBJECTION TO DRAWINGS SHOULD BE WITHDRAWN**

The drawings of the present application stand objected to as allegedly failing to comply with 37 C.F.R. 1.84. (See Office Action, p. 3). In particular, the Examiner contends that originally-filed Figure 2 appears to be a duplicate of Figure 1, and that Figure 2 is allegedly not described in the Specification. (*Id.*)

As the Examiner shall ascertain, the drawings have been amended as provided herein above and included on the attached Replacement Sheets merely to address a certain non-intentional error, and address the Examiner's comments in the Office Action. In particular, Figure 2 has been removed, and Figures 3 and 4 have been renumbered to be Figures 2 and 3, respectively.

Therefore, Applicants respectfully assert that the objection to the drawings is now moot, and should be withdrawn for at least the reasons provided herein above.

III. OBJECTION TO SPECIFICATION SHOULD BE WITHDRAWN

The Specification of the present application stands objected to as allegedly failing to comply with 37 C.F.R. 1.84. (*Id.*) In particular, the Examiner contends that there is no Brief Description of the Drawings. (*Id.*) As the Examiner shall ascertain, the Specification has been amended herein accordingly to provide a brief description of the drawings therein. Therefore, Applicants respectfully assert that the objection to the specification is now moot, and should be withdrawn for at least the reasons provided herein above.

Further, for consistency purposes, the Specification of the present application has been amended to change the figure numbers so as to correspond to the amendment to the drawings, as indicated herein above.

IV. REJECTION UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

Independent claim 1 stands rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. (See Office Action, p. 4). Additionally, claims 41-55 stand rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter (*Id.*, p. 5). Further, independent claims 83 stands rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter (*Id.*, p. 5). Applicants respectfully disagree, and respectfully assert that the pending claims

of the present application fully comply with the requirements of 35 U.S.C. § 101 for at least the following reasons.

A. Independent Claim 1

With respect to amended independent claim 1, the Examiner contends that the claimed subject matter does allegedly not require a tie to a specific machine. (*Id.*, p. 5.) Applicants respectfully disagree, and assert that one having ordinary skill in the art at the time the above-identified application was filed would understand that one or more of the procedures recited in independent claim 1 (as previously presented) inherently involve the use of a machine, such as a processing arrangement. Indeed, one having ordinary skill in the art would not even consider, much less attempt to perform one or more of the recited procedures of previously-pending claim 1 without the use of a machine. Accordingly, independent claim 1 (as previously presented) certainly recites statutory subject matter.

Nevertheless, in the interest of expediting the prosecution of the above-identified application and to address the Examiner's comments in the Office Action, but not for any reason relating to patentability thereof in view of 35 U.S.C. § 101, independent claim 1 has been amended as provided above to recite, *inter alia*, the use of a **hardware processing arrangement** (e.g., a processing arrangement which includes at least one hardware processor) in the producing procedure.

As described in the Federal Circuit decision of *In re Bilski*, recently affirmed by the Supreme Court, "[t]he machine-or-transformation test is a two-branched inquiry; an applicant may show that a process claim satisfies § 101 either by showing

that his claim is tied to a particular machine, or by showing that his claim transforms an article.” (*In re Bilski*, 545 F.3d 943, 961 (CA Fed. 2008) (*en banc*)). While the Supreme Court held that the “machine-or-transformation test” is not the sole test for deciding whether a claim is directed to a patent-eligible process under 35 U.S.C. §101, the Court held that “the machine-or-transformation test is a useful and important clue, an investigative tool, for determining whether some claimed inventions are processes under §101.” (*See Bilski v. Kappos*, 561 U. S. (2010) (decided June 28, 2010, Opinion, p. 8)). Indeed, the Court further held that “Section 101 similarly precludes the broad contention that the term process categorically excludes business methods” (*id.*, p. 10), thereby making clear that a process may qualify as patent eligible subject matter under §101 even if it fails to satisfy the machine-or-transformation test.

Thus, amended independent claim 1 certainly recites statutory subject matter, e.g., using a hardware processing arrangement in the producing procedure to produce one or more portions of the genome wide map, thereby **tying the method to a particular machine** and satisfying the machine-or-transformation test of *In re Bilski*.

Therefore, Applicants respectfully assert that the rejection of amended independent claim 1 under 35 U.S.C. § 101 is now moot, and should be withdrawn for at least the reasons described herein above.

B. Claims 41-55

With respect to independent claims 41 and 55 and claims 42-54 which depend from independent claim 41, the Examiner contends that these claims are

directed to software arrangements that allegedly are not required to be embodied on a computer. Applicants respectfully disagree with the Examiner regarding this rejection.

As an initial matter, each of independent claims 41 and 55 (as previously presented) explicitly recites a software arrangement which, when executed on a processing device, configures the processing device to perform certain procedures. Thus, independent claims 41 and 55 (as previously presented) are certainly not directed to software *per se*, but rather to software arrangements, which when executed on a processing device, configure the processing device to perform certain procedures.

Nevertheless, in the interest of expediting the prosecution of the above-identified application, independent claims 41 and 55, and claims 42-54 which depend from independent claim 41, have been amended as provided above to recite, *inter alia*, a **non-transitory** computer-accessible medium.

According to the Official Gazette notice 1351 OG 212 of February 23, 2010 entitled "Subject Matter Eligibility of Computer Readable Media" ("the OG Notice"),

A claim drawn to such a computer readable medium that covers both transitory and non-transitory embodiments may be amended to narrow the claim to cover only statutory embodiments to avoid a rejection under 35 U.S.C. § 101 by adding the limitation "non-transitory" to the claim. Cf. *Animals - Patentability*, 1077 Off. Gaz. Pat. Office 24 (April 21, 1987) (suggesting that applicants add the limitation "non-human" to a claim covering a multi-cellular organism to avoid a rejection under 35 U.S.C. § 101). Such an amendment would typically not raise the issue of new matter, even when the specification is silent because the broadest reasonable interpretation relies on the ordinary and customary meaning that includes signals *per se*. The limited situations in which such an amendment could raise issues of new matter occur, for example, when the specification does not support a non-transitory embodiment because a signal *per se* is the only viable embodiment such that the amended claim is impermissibly broadened beyond the

supporting disclosure. See, e.g., *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473 (Fed. Cir. 1998).

OG Notice, para. 2. Accordingly, Applicants respectfully assert that amended independent claims 41 and 55, and claims 42-54 which depend from independent claim 41, certainly recite statutory subject matter under 35 U.S.C. § 101.

Therefore, for at least the reasons described herein above and the reasons provided in the *OG Notice*, but not for any reason relating to patentability thereof in view of 35 U.S.C. § 101, Applicants respectfully assert that the rejection of amended claims 41-55 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter is now moot, and should be withdrawn.

C. Independent claim 83

With respect to independent claim 83, the Examiner admits that independent claim 83 recites a system comprising a storage medium including software that is executed to perform a process. (*Office Action*, p. 6). However, the Examiner still contends that the recited system is allegedly not limited to comprise any hardware elements such that it is interpreted to be a physical article of manufacture. (*Id.*)

Applicants respectfully disagree, and assert that one having ordinary skill in the art at the time the above-identified application was filed would understand that the system recited in independent claim 83 (as previously presented) inherently involve the use of a machine, such as a processing arrangement, to perform the process. Indeed, one having ordinary skill in the art would not even consider performing the recited

procedures without the use of a machine. Accordingly, independent claim 83 (as previously presented) certainly recites statutory subject matter.

Further, Applicants respectfully assert that the storage medium explicitly recited in independent claim 83 (as previously presented) is certainly statutory subject matter as defined under 35 U.S.C. § 101. However, the Examiner contends that the recited storage media is allegedly computer readable media that read on programs, *per se*, which are not statutory. Applicants respectfully disagree.

Nevertheless, to expedite the prosecution of the above-identified application and to address the Examiner's comments in the Office Action, independent claim 83 has been amended herein above to recite, *inter alia*, a **non-transitory storage medium**.

Therefore, for at least the reasons described herein above and the reasons provided in the OG Notice, but not for any reason relating to patentability thereof in view of 35 U.S.C. § 101, Applicants respectfully assert that the rejection of amended independent claim 83 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter is now moot, and should be withdrawn.

V. REJECTION UNDER 35 U.S.C. § 112, ¶2 SHOULD BE WITHDRAWN

Claims 1, 41-55 and 83 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. (See Office Action, p. 7).

A. Independent claims 1, 41, 55 and 83

In the Office Action, the Examiner contends that independent claims 1, 41, 55 and 83 (in procedure b) recite producing “a portion of the at least one genome wide map, where the at least one genome wide map comprises...”, and that there is no purportedly no previous step in the claims where a genome wide map has actually been produced. (Office Action, p. 7). For such purported reason, the Examiner believes that there is lack of antecedent basis for “a portion of the at least one genome wide map.” (*Id.*) Applicants respectfully assert that the subject matter recited in amended independent claims 1, 41, 55 and 83 is certainly not indefinite under 35 U.S.C. § 112, second paragraph, for at least the reasons described herein below.

Amended independent claim 1 recites, *inter alia*,

A process for producing one or more portions of a genome wide map, comprising:

- (a) receiving single DNA molecules maps derived from the DNA of a single individual; and
- (b) using a hardware processing arrangement, producing the one or more portions of the genome wide map based on the single DNA molecules maps, wherein the genome wide map comprises at least one of a haplotyped genome wide map or a genotyped genome wide map.

Amended independent claims 41 and 83 are directed to a computer-accessible medium and system, respectively, and recite similar subject matter as recited in amended independent claim 1.

Amended independent claim 55 recites, *inter alia*,

A non-transitory computer-accessible medium having stored thereon computer executable instructions-which, when the executable instructions

are executed on a processing device, configure the processing device to perform procedures comprising:

- (a) generate a haplotyped genome wide map per each individual one of at least one patient; and
- (b) perform a disease gene association based on the generated haplotyped genome wide map of each individual one of the at least one patient.

As an initial matter, Applicants bring to the Examiner's attention that there is no recitation of producing "a portion of the at least one genome wide map, where the at least one genome wide map comprises ..." in independent claim 55 (as previously presented or as amended).

Further, with respect to independent claims 1, 41 and 83, each of these claims have been amended to no longer recite the production of " a portion of the at least one genome wide map, where the at least one genome wide map comprises ...," the phrase the Examiner contends is the reason for this rejection of these claims. Rather, independent claims 1, 41 and 83 have been amended and now recite, *inter alia*, the production of "one or more portions of a genome wide map, wherein the genome wide map comprises"

Applicants respectfully assert that there is certainly proper antecedent basis for, e.g., **the genome wide map**, as recited in amended independent claims 1, 41 and 83 – i.e., the production of one or more portions of **a genome wide map**. Further, there is certainly also proper antecedent basis for **the generated haplotyped genome wide map** recited in procedure (b) – i.e., the generation of **a haplotyped genome wide map** recited in procedure (a).

B. Independent claims 41 and 55

In the Office Action, the Examiner further contends that independent claims 41 and 55 recite “the processing arrangement” in procedures (a) and (b) thereof for which there is allegedly insufficient antecedent basis (Office Action, p. 7). Applicants respectfully assert that amended independent claims 41 and 55 are certainly not indefinite under 35 U.S.C. § 112, second paragraph.

Indeed, as the Examiner shall ascertain, amended independent claim 41 recites, *inter alia*, the use of **a hardware processing arrangement**. Further, amended independent claim 55 recites, *inter alia*, the use of **a processing device**. Accordingly, Applicants respectfully assert that there is certainly proper antecedent basis both of a hardware processing arrangement and for a processing device, as recited in amended independent claims 41 and 55, respectively.

C. Claim 45

With further respect to claim 45 which depends from amended independent claim 41, the Examiner contends that the “wherein” clause and the use of passive language (i.e., is assembled) allegedly makes unclear what positive limitation of the claimed software arrangement is intended. (Office Action, p. 8).

Amended claim 45 recites that, *inter alia*, **the genome wide map comprises two maps per chromosome and is assembled from the at least one single molecule map data set.**

Applicants respectfully assert that amended claim 45 is certainly not indefinite under 35 U.S.C. § 112, second paragraph for at least the reasons provided herein. Indeed, as the Examiner shall ascertain, claim 45 has been amended and now recites that, *inter alia*, the genome wide map comprises “two maps per chromosome and is assembled” Accordingly, Applicants respectfully assert that amended claim 45 is certainly clear and not indefinite.

D. Claim 53

In the Office Action, the Examiner alleges that, with respect to the recitation in claim 53 of “the particular time is a sub-quadratic function”, it is purportedly unclear what limitation of the recited software arrangement is intended, and that the specification purportedly does not provide a limiting definition for a sub-quadratic function. (Office Action, p. 8). The Examiner indicates that “[t]his rejection could be overcome by amending the claims to recite, for example, a software arrangement wherein steps are performed using a sub-quadratic function to represent time.” (*Id.*)

Amended claim 53 recites that, *inter alia*, **the executable instructions further configure the processing device to perform steps (a) and (b) within a particular time limit, and that the particular time is bounded from above by a less than quadratic function of a number of sites associated with input data.**

While Applicants appreciate the suggestion by the Examiner in the Office Action indicated above, Applicants respectfully assert that amended claim 53 is certainly clear and not indefinite under 35 U.S.C. § 112, second paragraph. Indeed, claim 43 has been amended and now recites that, *inter alia*, **that the particular time is bounded**

from above by a less than quadratic function of a number of sites associated with input data. Applicants respectfully assert that one having ordinary skill in the art at the time the above-identified application was filed would certainly understand what limitation is intended (e.g., **the particular time is bounded from above by a less than quadratic function of a number of sites associated with an input data**).

Further, Applicants respectfully assert that, contrary to the Examiner's assertion in the Office Action, the specification certainly does provide a limiting definition for a sub-quadratic function. For example, the Specification of the originally-filed Application provides that, *inter alia*, “[g]eometric hashing can have sub-quadratic complexity in the worst case and the complexity may be as good as linear [and that t]he actual time for this state of computation is usually small compared to the time for the remaining search over possible H1 and H2.” (Specification, p. 12, Ins. 24-26).

Therefore, for at least the reasons provided herein above, Applicants respectfully assert that the rejection of amended independent claims 1, 41, 55 and 83, and claims 42-54 which depend from amended independent claim 41, under 35 U.S.C. § 112, second paragraph as allegedly being indefinite is now moot, and should be withdrawn.

VI. REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 1, 41-48, 55 and 83 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Lim et al., *Shotgun Optical Maps of the Whole Escherichia Coli 0157:H7 Genome*, Genome Res. 2001, vol. 11, pp. 1584-1593 (the

“Lim Publication”), in view of Buetow et al., *Integrated human genome-wide maps constructed using the CEPH reference panel*, Nature Genetics, 1994, vol. 6, pp. 3961-393 (the “Buetow Publication”). (See, e.g., Office Action, p. 9). Additionally, claims 51 and 52 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over the Lim Publication in view of the Buetow Publication and Cooke et al., *An integrated genetic map of Chromosome 6*, Mammalian Genome, 1996, vol. 7, pp. 157-159 (the “Cooke Publication”). (*Id.*, p. 13). Further, claims 49, 50, 53 and 54 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over the Lim Publication in view of the Buetow Publication, the Cooke Publication, Anantharaman et al., *Genomics via Optical Mapping II: Order Restriction Maps*, Optical Mapping, December 1996, pp. 1-41 (the “Anantharaman Publication”) and Kaltofen et al., *Subquadratic-Time Factoring of Polynomials Over Finite Fields*, Mathematics of Computation, 1998, vol. 67, no. 223, pp. 1179-1197 (the Kaltofen Publication”).

Applicants respectfully assert that the alleged combination of the Lim Publication and the Buetow Publication, even if combined with the Cooke Publication, the Anantharaman Publication and/or the Kaltofen Publication, fails to teach or suggest the subject matter recited in amended independent claims 1, 41, 55 and 83, and claims 42-54 which depend from amended independent claim 41, for at least the following reasons set forth herein below.

“To reject claims in an application under Section 103, an examiner must show an unrebutted *prima facie* case of obviousness.” *In re Rouffet*, 47 U.S.P.Q.2d

1453, 1455 (Fed. Cir. 1998). The Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966), stated:

Under Section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

Indeed, to sustain a rejection under 35 U.S.C. § 103(a), there must be some teaching, other than the instant application, to alter the prior art to arrive at the claimed invention. “The problem confronted by the inventor must be considered in determining whether it would have been obvious to combine the references in order to solve the problem.” *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1998).

The objective standard for determining obviousness under 35 U.S.C. § 103, as set forth in *Graham v. John Deere, Co.*, 383 U.S. 1 (1966), requires a factual determination to ascertain: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; and (3) the differences between the claimed subject matter and the prior art. Based on these factual inquiries, it must then be determined, as a matter of law, whether or not the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the alleged invention was made. *Graham*, 383 U.S. at 17. Courts have held that there must be some suggestion, motivation or teaching of the desirability of making the combination claimed by the applicant (the “TSM test”). See *In re Beattie*, 974 F.2d 1309, 1311-12 (Fed. Cir. 1992). This suggestion or motivation may be derived from the prior art itself, including references or disclosures that are known to be of special interest or importance in the field, or from

the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

Although the Supreme Court criticized the Federal Circuit's application of the TSM test, see *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, (2007) the Court also indicated that the TSM test is not inconsistent with the *Graham* analysis recited in the *Graham v. John Deere* decision. *Id.*; see *In re Translogic Technology, Inc.*, No. 2006-1192, 2007 U.S. App. LEXIS 23969, *21 (October 12, 2007). Further, the Court underscored that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, 127 S. Ct. at 1741. Under the precedent established in *KSR*, however, the presence or absence of a teaching, suggestion, or motivation to make the claimed invention is merely one factor that may be weighed during the obviousness determination. *Id.* Accordingly, the TSM test should be applied from the perspective of a person of ordinary skill in the art and not the patentee, but that person is creative and not an automaton, constrained by a rigid framework. *Id.* at 1742. However, "the reference[s] must be viewed without the benefit of hindsight afforded to the disclosure." *In re Paulsen*, 30 F.3d 1475, 1482 (Fed. Cir. 1994).

The prior art cited in an obviousness determination should create a reasonable expectation, but not an absolute prediction, of success in producing the claimed invention. *In re O'Farrell*, 853 F.2d. 894, 903-04 (Fed. Cir. 1988). Both the suggestion and the expectation of success must be in the prior art, not in applicant's disclosure. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1207 (Fed.

Cir. 1991) (citing *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988)). Further, the implicit and inherent teachings of a prior art reference may be considered under a Section 103 analysis. See *In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995).

Secondary considerations such as commercial success, long-felt but unsolved needs, failure of others, and unexpected results, if present, can also be considered. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-39 (Fed. Cir. 1983). Although these factors can be considered, they do not control the obviousness conclusion. *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988).

Absence of a property which a claimed invention would have been expected to possess based on the teachings of the prior art is evidence of nonobviousness. *Ex parte Mead Johnson & Co.* 227 USPQ 78 (Bd. Pat. App. & Inter. 1985). Evidence of unobvious or unexpected advantageous properties can rebut *prima facie* obviousness. *In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987).

To establish obviousness, the prior art references must be evaluated as a whole for what they fairly teach and neither the references' general nor specific teachings may be ignored. *Application of Lundsford*, 357 F.2d. 385, 389-90 (CCPA 1966). A reference must be considered for all that it teaches, not just what purportedly points toward the invention but also that which teaches away from the invention. *Ashland Oil, Inc. v. Delta Resins & Refractories*, 776 F.2d. 281, 296 (Fed. Cir. 1985).

Amended independent claim 1 recites, *inter alia*,

A process for producing one or more portions of a genome wide map, comprising:

- (a) **receiving single DNA molecules maps derived from the DNA of a single individual**; and
- (b) **using a hardware processing arrangement, producing the one or more portions of the genome wide map based on the single DNA molecules maps, wherein the genome wide map comprises at least one of a haplotyped genome wide map or a genotyped genome wide map.**

Amended independent claims 41 and 83 are directed to a computer-accessible medium and system, respectively, and recite similar subject matter as recited in amended independent claim 1.

Amended independent claim 55 recites, inter alia,

A non-transitory computer-accessible medium having stored thereon computer executable instructions—which, when the executable instructions are executed on a processing device, configure the processing device to perform procedures comprising:

- (a) **generate a haplotyped genome wide map per each individual one of at least one patient**; and
- (b) **perform a disease gene association based on the generated haplotyped genome wide map of each individual one of the at least one patient.**

The Lim Publication relates to, e.g., “shotgun optical maps of the whole Escherichia coli 0157:H7 genome.” (See, e.g., the Lim Publication, Title). For example, as described in this publication, NheI and XhoI optical maps of Escherichia coli 0157:H7 have been constructed solely from genomic DNA molecules to provide a uniquely valuable scaffold for contig closure and sequence validation. (*Id.*, Abstract).

The Buetow Publication relates to, e.g., the assembly of a collection of genetic maps constructed from primary data collected from investigators performing genotyping using the Centre Etude Polymorphism (CEPH) reference pedigree panel, which maps were constructed with the use of markers. (See, e.g., the Buetow Publication, Abstract).

Applicants respectfully assert that the Lim Publication and the Buetow Publication, taken alone or in combination, fail to teach or suggest process, computer-accessible medium or system for **receiving single DNA molecules maps derived from the DNA of a single individual and producing one or more portions of a genome wide map based on the single DNA molecules maps, where the genome wide map comprises at least one of a *haplotyped genome wide map* or a *genotyped genome wide map***, as explicitly recited in amended independent claims 1, 41 and 83 of the above-identified application. Further, Applicants respectfully assert that the Lim Publication and the Buetow Publication, taken alone or in combination, fail to teach or suggest at least the **generation of a haplotyped genome wide map per each individual one of at least one patient**; and the **performance of a disease gene association based on the generated *haplotyped genome wide map* of each individual one of the patient(s)**, as explicitly recited in amended independent claim 55 of the above-identified application.

As an initial matter, in the Office Action, the Examiner admits that “Lim does not teach a genome wide map comprising a haplotyped or genotyped genome wide map, as recited in independent claims 1, 41, 55 and 83.” (Office Action, p. 12).

However, the Examiner asserts that the Buetow Publication purportedly cures this admitted deficiency of the Lim Publication. Applicants respectfully disagree.

Indeed, the Buetow Publication describes assembling a collection of genetic maps constructed from primary data collected from investigators performing genotyping using the Centre Etude Polymorphism (CEPH) reference pedigree panel, which maps were constructed with the use of markers. (See, e.g., the Buetow Publication, Abstract).

However, even assuming, *arguendo*, that the alleged combination of the Lim Publication and the Buetow Publication teaches and/or suggests producing genome wide map comprising a haplotyped genome wide map and/or a genotyped genome wide map (contention Applicants respectfully disagree), it cannot be disputed that neither the Lim Publication nor the Buetow Publication teach or suggest the **production of one or more portions of a genome wide map based on the single DNA molecules maps derived from the DNA of a single individual, where the genome wide map comprises a haplotyped genome wide map and/or a genotyped genome wide map**, as explicitly recited in amended independent claims 1, 41 and 83 of the above-identified application. Indeed, the Examiner does contend that these publications teach, suggest or disclose such recited subject matter. Similarly, neither the Lim Publication nor the Buetow Publication teach or suggest the **generation of a haplotyped genome wide map for each individual one of at least one patient and the performance of a disease gene association based on the generated haplotyped genome wide map of each individual one of the patient(s)**, as explicitly recited in amended independent

claim 55 of the above-identified application, and the Examiner does not contend that these publications teach or suggest such recited subject matter.

In addition, Applicants respectfully assert that the Cooke Publication, the Anantharaman Publication and the Kaltofen Publication fail to cure at least the above-described deficiencies of the alleged combination of the Lim Publication and the Buetow Publication, and the Examiner does not assert that they do.

Further, contrary the assertion by the Examiner on page 12 of the Office Action, Applicants respectfully assert that it would not have been obvious for one having ordinary skill in the art at the time the above-identified application was filed to modify the genome wide maps allegedly taught by the Lim Publication by including the use of genotyped markers described in the Buetow Publication with a reasonable expectation of success. The Examiner contends that one having ordinary skill in the art would have been aware of methods for integrating a plurality of genotyped markers into genome wide maps and have been purportedly motivated to improve maps for disease-based linkage studies based on p.393, col. 2 of the Buetow Publication. (See Office Action, p. 12, last para.). However, the Lim Publication and the Buetow Publication utilize different types of information and methods to solve different problems. For example, as indicated herein above, the Lim Publication relates to, e.g., shotgun optical maps of the whole *Escherichia coli* O157:H7 genome (see, e.g., Lim Publication, Title), while the Buetow Publication relates to, e.g., Integrated human genome-wide maps constructed using the CEPH reference panel (see, e.g., Buetow Publication, Title). Thus, not only would it have not been obvious to combine the teachings of these publications, both the

Lim Publication and the Buetow Publication actually **teach away** from being combined with one another, and certainly not to solve the problem using, e.g., the method(s), computer-accessible medium and system(s) recited in amended claims 1, 41, 55 and 83 of the present application.

As discussed above, a reference must be considered for all that it teaches, not just what purportedly points toward the invention but also that which teaches away from the invention. *Ashland Oil, Inc. v. Delta Resins & Refractories*, 776 F.2d 281, 296 (Fed. Cir. 1985). Further, the Supreme Court in *KSR International*, stated that “when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious.” *KSR*, 127 S. Ct. at 1740. Moreover, “[t]he problem confronted by the inventor must be considered in determining whether it would have been obvious to combine the references in order to solve the problem.” *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1998).

Therefore, for at least the reasons described herein above, the rejection of amended independent claims 1, 41, 55 and 83, and claims 42-54 which depend from amended independent claim 41, under 35 U.S.C. § 103(a) as allegedly being unpatentable over the alleged combination of the Lim Publication and the Buetow Publication, taken alone or in combination with the Cooke Publication, the Anantharaman Publication and the Kaltoven Publication, should be withdrawn.

VII. NEW CLAIMS

New claims 123-138 have been added above to recite certain subject matter which Applicants believe includes novel features and is separately patentable. Support for new claims 123-138 can be found in the originally-filed application, including the specification, drawings and/or claims thereof. (See, e.g., Specification of the above-identified application, p. 12, ln. 13 – p. 13, ln. 8, and originally-filed claims 1, 14, 15, 20, 41-55 and 83).

In particular, new claims 123-132 depend from amended independent claims 1, 41, 55 and 83, as applicable. Further, new independent claims 133 and 136 are directed to process and system, respectively, and recite similar subject matter as recited in amended independent claim 55. New claims 134 and 135 depend from new independent claim 133, and new claims 137 and 138 depend from new independent claim 136.

Thus, Applicants respectfully assert that new claims 123-138 are allowable over the alleged combination of the Lim Publication and the Buetow Publication, even if combined with the Cooke Publication, the Anantharaman Publication and the Kaltofen Publication, for at least the reasons described herein above with respect to amended independent claims 1, 41, 55 and 83.

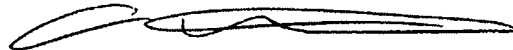
In addition, Applicants respectfully assert that new claims 123-138 include subject matter which is separately patentable from the recitations of amended independent claims 1, 41, 55 and 83, and the claims which depend therefrom.

VIII. CONCLUSION

In light of the foregoing, Applicant respectfully submits that pending claims 1, 41-55, 83 and 123-138 are in condition for allowance. Prompt consideration, reconsideration and allowance of the present application are therefore earnestly solicited. If any issues remain outstanding, the Examiner is invited to contact the undersigned via the telephone number provided below.

To the extent any additional claim fees and extension of time fees are due, Applicants believe that the fees have been paid in connection with the submission of this paper, as needed. However, if any additional fee is due, or if any overpayment has been made, the Commissioner is authorized to charge any such fee, or credit any overpayment, to Deposit Account No. 50-2054.

Respectfully submitted,



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By: _____

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